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**PRIMARY EYE IRRITATIONS  
IN THE RABBIT**

**FINAL REPORT**

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IITRI Project No. L8100  
Study No. 55  
Test Article No. 14

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IIT Research Institute  
Life Sciences Research  
10 West 35th Street  
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Chicago, IL 60601

Nov 9, 1980

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IITRI Project No. L8100

**PRIMARY EYE IRRITATION STUDY OF  
IN THE RABBIT  
Study No. 55  
Test Article No. 14**

This report summarizes a primary eye irritation study conducted by IIT Research Institute for the Standard Oil Co. (Indiana).

Bruce K. Bernard, Senior Toxicologist, served as study director and was responsible for the overall conduct of the study. Gerald King, Assistant Toxicologist, was responsible for the collection of test data. Calvin Reaves, Experimentalist was responsible for animal care personnel. Josephine M. Reed, Supervisor, Quality Assurance, was responsible for the quality assurance program.

*Bruce K. Bernard 5/9/80*

Bruce K. Bernard      Date  
Study Director  
Program Director  
Life Sciences Research

*Richard Ehrlich 5/19/80*

Richard Ehrlich      Date  
Director  
Life Sciences Research

*Josephine M. Reed 4/28/80*

Josephine M. Reed      Date  
Supervisor Quality Assurance  
Life Sciences Research

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**PRIMARY EYE IRRITATION STUDY OF  
IN THE RABBIT  
Study No. 55  
Test Article No. 14**

**SUMMARY**

A single dose of 0.1 ml of \_\_\_\_\_ was instilled into the right eye of each of six (6) rabbits. Corneal opacities were observed in six rabbits at the 24 and 48 hour observation interval; the number of rabbits with opacities decreased to 5, 4 and 0 at 72, 96 and 168 hours after dosing. Iritis was observed in four rabbits at 24 hours and one rabbit at 48 hours. Six rabbits showed varying degrees of chemosis and erythema while five rabbits showed discharge at the 24 hour observation. All rabbits exhibited what is considered to be a positive reaction.

The maximum Primary Irritation Score was 40.3 at 24 hours after dosing. The scores declined at each interval thereafter to a minimum score of 0 at the final observation (168 hours).

Under the guidelines of the Federal Hazardous Substances Act, \_\_\_\_\_ is considered to be a primary eye irritant.

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PRIMARY EYE IRRITATION STUDY OF  
IN THE RABBIT

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I. INTRODUCTION

The purpose of this study was to evaluate the primary eye irritation potential of \_\_\_\_\_ in rabbits.

II. MATERIALS AND METHODS

a. Test Article. (lot no. A-013-J9; approximately one gallon (3.8 l); gross weight of 3.54 kg) was received December 4, 1979. The original polyethylene container and contents were stored in a ventilated cabinet at room temperature (approximately 22°C). A reserve sample of 10 ml was taken at the time of study initiation and stored under identical conditions.

b. Dosage Formulation. The test article was instilled undiluted.

c. Animals, Housing and Diet. New Zealand albino rabbits (Lesser's Rabbitry, Union Grove, Wisconsin), were used for this study. Upon arrival (1/16/80), the rabbits were housed individually in stainless steel cages. The cage size (61.0 x 45.5 x 42.0 cm) conformed to the upper limit weight range recommended in the *Guide for the Care and Use of Laboratory Animals*, DHEW, (NIH) No. 78.23. Air conditioned rooms were maintained at 22 ± 1°C and approximately 40% relative humidity. Fluorescent lighting was provided on a 12-hour light-dark cycle. Purina Rabbit Chow and tap water (supplied by an automatic watering system) were available *ad libitum*.

d. Experimental Design. The test article was instilled into the right eye of each of six (6) rabbits; the left eye remained untreated as a control.

e. Method. Prior to study initiation, the rabbits were observed during a quarantine period of two weeks. One day prior to study

initiation, the rabbits were examined for general health and for corneal lesions with the aid of 2% sodium fluorescein (Aldrich Chemicals, Milwaukee, Wisconsin), and ultraviolet light. Six (6) rabbits (3 male, 3 female) were chosen for inclusion in the study. The rabbits were given a unique number tag inserted into the right ear. A card on the front of each cage bore the study number, test article number, animal number, dose, sex and date of arrival.

On the day of study initiation (2/4/80), 0.1 ml of the test article was instilled into the everted lower lid of the right eye of each rabbit.

f. Animal Weights. The rabbits were weighed and weights recorded immediately prior to dosing. The weight range for the rabbits was 2.4 to 2.9 kg.

g. Mortality. The rabbits were observed daily for mortality and morbidity.

h. Ocular Examinations. The eyes of each test rabbit were examined 24, 48, 72, 96 and 168 hours after test article administration. At each interval, ocular lesions were scored according to the method of Draize (Appendix I), and results recorded. The cornea was observed for appearance and extent of opacity; the iris for congestion, swelling, circumcorneal injection, and reaction to light; and the conjunctiva for erythema, chemosis and discharge.

The scores were tabulated by interval and scoring category. Mean scores per category were calculated and the resulting mean scores summed.

i. Animal Disposition. The rabbits were sacrificed humanely and discarded at the completion of the study.

### III. RESULTS

a. Mortality. No mortality was observed during the 168 hour observation period.

b. Ocular Lesions. The individual irritation scores (Appendix II) were tabulated in Table 1. Corneal opacities were observed in six rabbits at the 24 and 48 hour observation interval; the number of rabbits with

opacities decreased to 5, 3 and 0 at 72, 96 and 168 hours after dosing. Iritis was observed in four rabbits at 24 hours and one rabbit at 48 hours. Six rabbits showed varying degrees of chemosis and erythema while five rabbits showed discharge at the 24 hour observation. Thereafter, all conjunctival categories showed a trend toward recovery culminating in the normal appearance of all rabbits at the 168 hour observation.

c. Primary Irritation Scores. The primary eye irritation scores are shown in Table 2.

According to the Federal Hazardous Substances Act, the test article is considered a primary eye irritant if four (4) or more of the six (6) test rabbits exhibit a positive reaction. A rabbit is considered to exhibit a positive reaction if, at any observation interval, the test article produces ulceration or opacity of the cornea (any cornea value greater than 0), inflammation of the iris, or slight circumcorneal injection of blood vessels (any iris value greater than 0), or any obvious conjunctival swelling with partial eversion of the lids (a chemosis value of two (2) or greater), or conjunctival erythema of diffuse crimson red with individual vessels not easily discernible (an erythema value of two (2) or greater).

During the course of the study, all rabbits exhibited a positive reaction. Therefore, is considered to be a primary eye irritant.

#### IV. QUALITY ASSURANCE

Raw data and final draft report were audited on April 25, 1980. All audits and inspections were conducted by Josephine M. Reed and studies were found to be in compliance with Life Sciences Quality Assurance criteria. Raw data generated during the course of this study will be maintained in the Life Sciences Archives as specified by government regulations.

Study Number: 55 Test Article Number: 14DOSE 0.1 ml  
Neat Material

## SUMMATION OF EYE IRRITATION SCORES

TABLE 1

OBSERVATION INTERVALS:  
(Hours)

## I. CORNEA

A. DENSITY OF  
OPACITY

	24	48	72	96	168
0	0	0	1/6	2/6	6/6
1	4/6	4/6	5/6	4/6	0
2	2/6	2/6	0	0	0
3	0	0	0	0	0
4	0	0	0	0	0

B. AREA OF  
OPACITY

1	0	0	0	0	0
2	0	0	1/6	1/6	0
3	0	0	0	1/6	0
4	6/6	6/6	4/6	2/6	0

## II. IRIS

0	2/6	5/6	6/6	6/6	6/6
1	4/6	1/6	0	0	0
2	0	0	0	0	0

## III. CONJUNCTIVA

## A. ERYTHEMA

0	0	1/6	3/6	4/6	6/6
1	4/6	4/6	3/6	2/6	0
2	1/6	1/6	0	0	0
3	1/6	0	0	0	0

## B. CHEMOSIS

0	0	0	2/6	2/6	6/6
1	3/6	6/6	4/6	4/6	0
2	0	0	0	0	0
3	3/6	0	0	0	0
4	0	0	0	0	0

## C. DISCHARGE

0	1/6	5/6	6/6	6/6	6/6
1	1/6	1/6		0	0
2	3/6	0	0	0	0
3	1/6	0	0	0	0

PRIMARY EYE IRRITATION (RABBIT)

PUBLIC COPY

Study Number: 55

Test Article Number: 14

DOSE 0.1 ml  
Neat Material

PRIMARY IRRITATION SCORES

TABLE

OBSERVATION INTERVALS:  
(Hours)

24	48	72	96	162
----	----	----	----	-----

I. CORNEA

A	8/5	8/5	5/5	4/6	0
B	24/6	24/6	18/6	13/6	0
TOTAL = (A)x(B)x5 =	960/36	960/36	450/36	260/36	0

II. IRIS

A	4/6	1/6	0	0	0
TOTAL = (A)x5x6/6 =	20/6 = 120/36	5/6 = 30/36	0	0	0

III. CONJUNCTIVA

A	9/6	6/6	3/6	2/6	0
B	12/6	6/6	4/6	4/6	0
C	10/6	1/6	0	0	0
TOTAL = (A+B+C)x2x6/6 =	62/6 = 372/36	26/6 = 156/36	14/6 = 84/36	12/6 = 72/36	0

TOTAL SCORE = (I+II+III) =

1452/36 = 40.3	1146/36 = 31.8	534/36 = 14.8	332/36 = 9.2	0
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APPENDICES

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## APPENDIX I

## TABLE I

SCALE FOR SCORING OCULAR LESIONS

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(1) Cornea		
(A)	Opacity-degree of density (area most dense taken for reading)	
	No opacity	0
	Scattered or diffuse area, details of iris clearly visible	1
	Easily discernible translucent areas, details of iris slightly obscured	2
	Opalescent areas, no details of iris visible, size of pupil barely discernible	3
	Opaque, iris invisible	4
(B)	Area of cornea involved	
	One quarter (or less) but not zero	1
	Greater than one quarter, but less than half	2
	Greater than half, but less than three quarters	3
	Greater than three quarters, up to whole area	4
	Score equals A x B x 5	Total Maximum = 80
(2) Iris		
(A)	Values	
	Normal	0
	Folds above normal, congestion, swelling, circumcorneal injection (any or all of these or combination of any thereof) iris still reacting to light (sluggish reaction is positive)	1
	No reaction to light, hemorrhage, gross destruction (any or all of these)	2
	Score equals A x 5	Total Maximum = 10
(3) Conjunctivae		
(A)	Redness (refers to palpebral and bulbar conjunctivae excluding cornea and iris)	
	Vessels normal	0
	Vessels definitely injected above normal	1
	More diffuse, deeper crimson red, individual vessels not easily discernible	2
	Diffuse beefy red	3
(B)	Chemosis	
	No swelling	0
	Any swelling above normal (Includes nictitating membrane)	1
	Obvious swelling with partial eversion of lids	2
	Swelling with lids about half closed	3
	Swelling with lids about half closed to completely closed	4
(C)	Discharge	
	No discharge	0
	Any amount different from normal (does not include small amounts observed in inner canthus of normal animals)	1
	Discharge with moistening of the lids and hairs just adjacent to lids	2
	Discharge with moistening of the lids and hairs, and considerable area around the eye	3
	Score equals (A + B + C) x 2	Total Maximum = 20

The maximum total score is the sum of all scores obtained for the cornea, iris, and conjunctivae. Total maximum score possible = 110

\* Draize, J.H., Appraisal of the Safety of Chemicals in Foods, Drugs, and Cosmetics, Assoc. Food and Drug Officials of the U.S., Austin, TX, 1959.

APPENDIX II  
PRIMARY EYE IRRITATION (RABBIT)

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S.N. 55

T.A. 14

DOSE 0.1 ml  
rest normal

INITIAL APPLICATION 2-4-80 1:48pm-1:50pm JK  
DATE TIME INITIAL

CONJUNCTIVA			IRIS	CORNEA	
DISCHARGE	CHEMOSIS	ERYTHEMA		OPACITY	AREA

DATE	TIME
2/5/80	1:35P
2/6/80	1:44P
2/7/80	1:19P
2/8/80	1:16P
2/11/80	1:10P

INDIVIDUAL IRRITATION SCORES

DISCHARGE	CHEMOSIS	ERYTHEMA	IRIS	OPACITY	AREA	INITIAL
2	3	1	0	1	4	JK
0	1	1	0	1	4	JK
0	1	1	0	1	2	JK
0	1	0	0	0	0	JK
0	0	0	0	0	0	JK

ANIMAL No. 76  
SEX M  
INITIAL Wt 2.6 kg

OBSERVATIONS:

DATE	TIME
2/5/80	1:40P
2/6/80	1:22P
2/7/80	1:21P
2/8/80	1:17P
2/11/80	1:11P

DISCHARGE	CHEMOSIS	ERYTHEMA	IRIS	OPACITY	AREA	INITIAL
0	1	1	1	1	4	JK
1	1	1	0	1	4	JK
0	0	0	0	0	0	JK
0	0	0	0	0	0	JK
0	0	0	0	0	0	JK

ANIMAL No. 77  
SEX M  
INITIAL Wt 2.5 kg

OBSERVATIONS:

DATE	TIME
2/5/80	1:45P
2/6/80	1:30P
2/7/80	1:23P
2/8/80	1:19P
2/11/80	1:17P

DISCHARGE	CHEMOSIS	ERYTHEMA	IRIS	OPACITY	AREA	INITIAL
2	3	1	1	2	4	JK
0	1	1	0	2	4	JK
0	1	1	0	1	4	JK
0	1	1	0	1	2	JK
0	0	0	0	0	0	JK

ANIMAL No. 78  
SEX M  
INITIAL Wt 2.4 kg

OBSERVATIONS:

READ AND UNDERSTOOD

B.L.P.  
DATE 4/19/80

REVIEWED BY B. Meyer 3/13/80

L81005N55

APPENDIX II (con't)  
PRIMARY EYE IRRITATION (RABBIT)

S.N. 55

T.A. 14

DUPON IC CO.®

DOSE 0.1ml  
nest material

INITIAL APPLICATION: 2-4-80 1:44pm JK  
DATE TIME INITIAL

CONJUNCTIVA			IRIS	CORNEA	
DISCHARGE	CHEMOSIS	ERYTHEMA		OPACITY	AREA

INDIVIDUAL IRRITATION SCORES

ANIMAL No. 73  
SEX F  
INITIAL Wt. 2890g

DATE	TIME
2/5/80	1:15P
2/6/80	1:16
2/7/80	1:10P
2/8/80	1:10P
2/9/80	1:05P

2	1	2	1	1	4	JK
0	1	1	0	1	4	JK
0	1	1	0	1	4	JK
0	1	1	0	1	4	JK
0	0	0	0	0	0	JK

OBSERVATIONS:

ANIMAL No. 74  
SEX F  
INITIAL Wt. 2768.4

DATE	TIME
2/5/80	1:25P
2/6/80	1:22
2/7/80	1:14P
2/8/80	1:10P
2/9/80	1:07P

3	3	3	1	2	4	JK
0	1	2	1	2	4	JK
0	0	0	0	1	4	JK
0	0	0	0	1	4	JK
0	0	0	0	0	0	JK

OBSERVATIONS:

ANIMAL No. 75  
SEX F  
INITIAL Wt. 2.5kg

DATE	TIME
2/5/80	1:30P
2/6/80	1:29
2/7/80	1:16P
2/8/80	1:13P
2/9/80	1:09P

1	1	1	0	1	4	JK
0	1	0	0	1	4	JK
0	1	0	0	1	4	JK
0	1	0	0	1	3	JK
0	0	0	0	0	0	JK

OBSERVATIONS:

REVIEWED BY B. Meyer 3/13/80 A-3

READ AND UNDERSTOOD

BKB  
DATE 4/19/80

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